

**Methods:** Electroacupuncture (EA) was applied at acupoints ST36 and GB39 of 61 healthy adults. Different coping conditions were experimentally designed to form an active coping strategy group (AC group), who thought they could control EA stimulation intensity, and a passive coping strategy group (PC group), who did not think they had such control. Importantly, neither group was actually able to control EA stimulus intensity. Quantitative sensory testing was performed before and after EA, and consisted of vibration (VDT), mechanical (MDT), warm (WDT), and cold (CDT) detection thresholds, and pressure (PPT), mechanical (MPT), heat (HPT) and cold (CPT) pain thresholds. Autonomic measures (e.g. skin conductance response, SCR) were also acquired to quantify physiological response to EA under different coping conditions. Subjects also reported the intensity of any acupuncture-induced sensations.

**Results:** Coping strategy was induced with successful blinding in 58% of AC subjects. Compared to PC, AC showed greater SCR to EA. Under AC, EA reduced PPT and CPT. In the AC group, improved pain and sensory thresholds were correlated with acupuncture sensation (VDTchange vs. MI:  $r = 0.58$ , CDTchange vs. tingling:  $r = 0.53$ , CPTchange vs. tingling:  $r = 0.55$ , CPTchange vs. dull:  $r = 0.55$ ). However, in the PC group, improved sensory thresholds were negatively correlated with acupuncture sensation (CDTchange vs. intensity sensitization:  $r = -0.52$ , WDTchange vs. fullness:  $r = -0.57$ ).

**Conclusions:** Our novel approach was able to successfully induce AC and PC strategies to EA stimulation. The interaction between psychological coping strategy and acupuncture sensation intensity can differentially modulate pain and sensory detection threshold response to EA. In a clinical context, our findings suggest that instructions given to the patient can significantly affect therapeutic outcomes and the relationship between acupuncture intensity and clinical response. Specifically, acupuncture analgesia can be enhanced by matching physical stimulation intensity with psychological coping strategy to acupuncture contexts.

**Keywords:** coping strategy, acupuncture, acupuncture sensation, pain, sensory threshold

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## Effects of Chronic Electroacupuncture on Depression- and Anxiety-like Behaviors in Rats with Chronic Neuropathic Pain

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### Abstract

Growing evidence indicates that chronic neuropathic pain is frequently accompanied by an array of psychiatric diseases, such as depression and anxiety. Electroacupuncture (EA), as one therapy of traditional Chinese medicine, has displayed potent antidepressant-like effects in numerous clinical studies. The present study was designed to examine the possible effects of EA on the depressive and anxiety disorders induced by neuropathic pain. A classic rat model of neuropathic pain was produced by chronic constriction injury (CCI) of the sciatic nerve. EA was performed on acupoints "Bai-Hui" (GV20) and unilateral "Yang-Ling-Quan" (GB34). The antidepressive and anxiolytic effects of EA treatment were analyzed using the forced swimming test (FST) and the elevated plus maze (EPM) test, respectively. CCI resulted in remarkable depression- and anxiety-like behaviors, whereas the chronic EA treatment significantly improved the behavioral deficits of CCI rats. Moreover, the phosphorylation level of the NMDA receptor type 1 (NR1) subunit was decreased in the hippocampus of CCI rats. Intriguingly, continuous EA treatment effectively blocked this decrease in the levels of pNR1. These results suggested that EA has antidepressive and anxiolytic effects on rats with neuropathic pain and that this might be associated with restoring the phosphorylation of NR1 in the hippocampus.

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## Effects of *Salviae Miltiorrhizae Radix* Hot Aqueous Extract on Nitric Oxide and Prostaglandin E2 Production and on 1,1-diphenyl-2-picryl hydrazyl Radical Scavenging in Macrophages

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## Abstract

**Objectives:** The objective of this study is to investigate the effects of *Salviae Miltiorrhizae Radix* hot aqueous extract on nitric oxide (NO) and prostaglandin E2 (PGE2) production and on 1,1-diphenyl-2-picryl hydrazyl (DPPH) free-radical scavenging in macrophages.

**Methods:** *Salviae Miltiorrhizae Radix* (300 g) was heated at 100°C with distilled water (2 L) for 4 hours. The extract was filtered and concentrated to 100 mL by using a rotary evaporator, was frozen at -80°C, and was then freeze-dried by using a freezing-drying system. The RAW 264.7 macrophage was subcultured by using 10-µg/mL lipopolysaccharide (LPS). In order to evaluate cytotoxicity, we performed (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) (MTT) assays and measured the cell viability. The NO production was measured by using Griess assays, and the PGE2 production was measured by using enzyme immunoassays. The antioxidant activity, the 1,1-diphenyl-2-picryl hydrazyl (DPPH) free-radical scavenging capability, was measured by using the DPPH method.

**Results:** Cell viability with the 1-, 5-, 25-, 125- and 625-µg/mL *Salviae Miltiorrhizae Radix* hot aqueous extract was not significantly decreased compared to the cell viability without the extract. When 125 and 625 µg/mL of *Salviae Miltiorrhizae Radix* hot aqueous extract were used, nitric oxide (NO) production in LPS-stimulated RAW 264.7 macrophages was significantly inhibited compared to that in the control group. When 25, 125, and 625 µg/mL of *Salviae Miltiorrhizae Radix* hot aqueous extract were used, PGE2 production in LPS-stimulated RAW 264.7 macrophages was significantly inhibited compared to that in the control group. The 125- and 625-µg/mL *Salviae Miltiorrhizae Radix* hot aqueous extracts had high DPPH free-radical scavenging capabilities in RAW 264.7 macrophages.

**Conclusion:** This study indicates that *Salviae Miltiorrhizae Radix* hot aqueous extract suppresses NO and PGE2 production and improves DPPH free-radical scavenging capability. Thus, it seems that *Salviae Miltiorrhizae Radix* hot aqueous extract may have an anti-inflammation effect and antioxidant activity.

**Keywords:** anti-inflammation, antioxidant activity, hot aqueous extract, Korean medicine, *Salviae Miltiorrhizae Radix*

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### Serum Biochemical, Histopathology and SEM Analyses of the Effects of the Indian Traditional Herb *Wattakaka Volubilis* Leaf Extract on Wistar Male Rats

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## Abstract

**Objectives:** The present study investigated the protective effect of *Wattakaka* (W.) *volubilis* leaf extract against streptozotocin (STZ)-induced diabetes in rats.

**Methods:** Male Wistar rats were divided into five groups (with six rats in each group) and were fed ad libitum. The rats were fasted for sixteen hours before diabetes was induced by injecting a single dose of 90 mg/kg body weight of STZ in 0.9-percent normal saline through an intraperitoneal route. The five groups were as follows: Group 1: normal control (saline-treated), Group 2: untreated diabetic rats, Groups 3 and 4: diabetic rats treated orally with petroleum ether cold maceration extract (PEME) of *W. volubilis* (50 and 100 mg/kg body weight), and Group 5: diabetic rats treated orally with metformin (250 mg/kg body weight). All rats received treatment for 21 days. For the STZ-induced diabetic rats, the blood-glucose,  $\alpha$ -amylase, total protein and alanine transaminase (ALT) levels were measured on days 7, 14 and 21 of the treatment with PEME of *W. volubilis* and the treatment with metformin. Histopathological changes in the liver were examined with hematoxylin-eosin staining. Morphological changes in the liver were also examined with glutaraldehyde fixation.

**Results:** The treatments with PEME of *W. volubilis* and with metformin in experimental rats by oral injections for 21 days produced reductions in the levels of serum biochemical markers. Histopathology and scanning electron microscopy results showed that the administrations of PEME of *W. volubilis* and of metformin suppressed the generation of abnormal liver cells in the STZ-treated rats.

**Conclusion:** These results suggest that both PEME of *W. volubilis* and metformin have a protective effect against STZ-induced diabetes.

**Keywords:** *Wattakaka volubilis*, petroleum ether cold maceration extract, streptozotocin, liver, scanning electron microscopy

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